

U.S. Application No. 10/529,889
Reply to August 21, 2008 Office Action
Response dated February 23, 2009

REMARKS

Claims 1-12 were pending in the present application. By this Amendment, Applicant has amended claim 1 and canceled claims 10 and 12. The cancellation of subject matter is without prejudice to Applicant's right to present such subject matter in a future continuing application. The present amendment does not introduce any new matter and thus its entry is respectfully requested. Upon entry of the present amendment, claims 1-9, and 11, will be pending and under examination.

August 21, 2008 Office Action

Species Election Requirement Withdrawn

The Office Action indicates that the Examiner found Applicant's previously elected species free of the art, expanded the search to include claims 1-12 in their entirety, and withdrew the election requirement.

In response, Applicant acknowledges and appreciates the withdrawal of the species election requirement.

Information Disclosure Statement

The Office Action indicated that certain documents listed on Applicant's Information Disclosure Statement filed April 1, 2005 were not available to the Examiner and thus have not been considered. The Office Action stated that Applicant may submit the missing references

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with the response to the Office Action and that no fee for such submission will be required.

In response, Applicants attach hereto copies of the four references the Examiner has indicated were missing. Applicants respectfully request that these references now be considered.

Claim Rejection Under 35 U.S.C. §112, first paragraph

Claims 10 and 12 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner's full rationale for the rejection is set forth at pages 3-7 of the Office Action.

In response, without conceding the correctness of the Examiner's position, but to expedite allowance of the application, Applicant has canceled claims 10 and 12 without prejudice, rendering the rejection moot. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 10 and 12 under 35 U.S.C. §112, first paragraph.

Claim Rejections Under 35 U.S.C. §112, second paragraph, and 35 U.S.C. §101

Claims 10 and 12 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite, and under 35 U.S.C. §101, as allegedly failing to set forth proper process steps. The Examiner's full rationales for the rejections are set forth at pages 7-8 of the Office Action.

In response, without conceding the correctness of the Examiner's positions, but to expedite allowance of the application, Applicant has canceled claims 10 and 12 without prejudice, rendering the rejections moot. Accordingly, Applicant respectfully requests

reconsideration and withdrawal of the rejections of claims 10 and 12 under 35 U.S.C. §112, second paragraph, and 35 U.S.C. §101.

Examiner's Rejections Under 35 U.S.C. §102(b)

Claims 1 and 7-12 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Ashley (U.S. Pat. No. 5,855,910). According to the Examiner, "Ashley teaches Applicants' compound of formula I where in R^1 =diacylglycerol R^2 =choline . . . and $R^3=C_1-C_{24}$ straight chain alkyl or alkenyl."

The Examiner further asserted that "Ashley teaches that these phospholipids can be obtained from the parent phosphoglyceride." The Examiner also stated that Ashley teaches a class of cationic phospholipids, and the synthesis thereof, that are capable of generating liposomes. According to the Examiner, the liposomes are taught as methods of treatment of diseases or ailments amenable to treatment with nucleic acids or oligonucleotides.

The Examiner also rejected claims 1 and 4 under 35 U.S.C. §102(b) as allegedly anticipated by Bruzik, et al. According to the Examiner, Bruzik teaches the synthesis of glycerophospholipids wherein R^1 =diacylglycerol, R^2 =glycerol, and $R^3=$ Me.

In response, without conceding the correctness of the Examiner's positions, but to expedite allowance of the present application, Applicant has amended claim 1 to recite ". . . and each of R^2 and R^3 is a residue independently selected from ethanolamine, N-methylethanolamine, propanolamine, choline, glycerol, oligoglycerols, glycoglycerols or serine . . ." The claims, as amended, are not anticipated by either reference cited by the Examiner and

U.S. Application No. 10/529,889
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thus, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b).

Allowable Subject Matter

The Examiner indicated that claims 2, 3, 5, and 6 were objected to as being dependent on a rejected base claim, but would be allowable if rewritten in independent form.

In response, Applicant acknowledges and appreciates the indication of allowable subject matter.

In light of the amendments and remarks presented herein, Applicant believes all of the rejections set forth in the August 21, 2008 Office Action have been fully overcome and the claims are in condition for allowance. The Examiner is invited to telephone the undersigned if it is deemed to expedite such allowance.

Respectfully submitted,

By _____

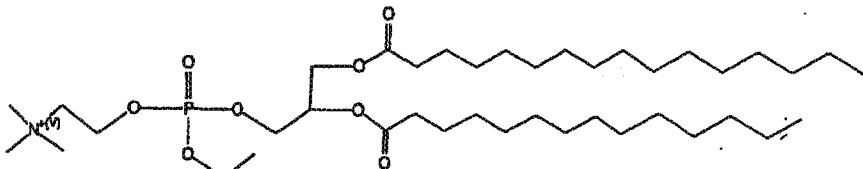
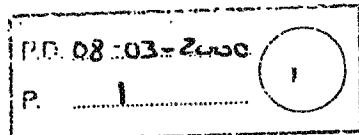


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February 23, 2009

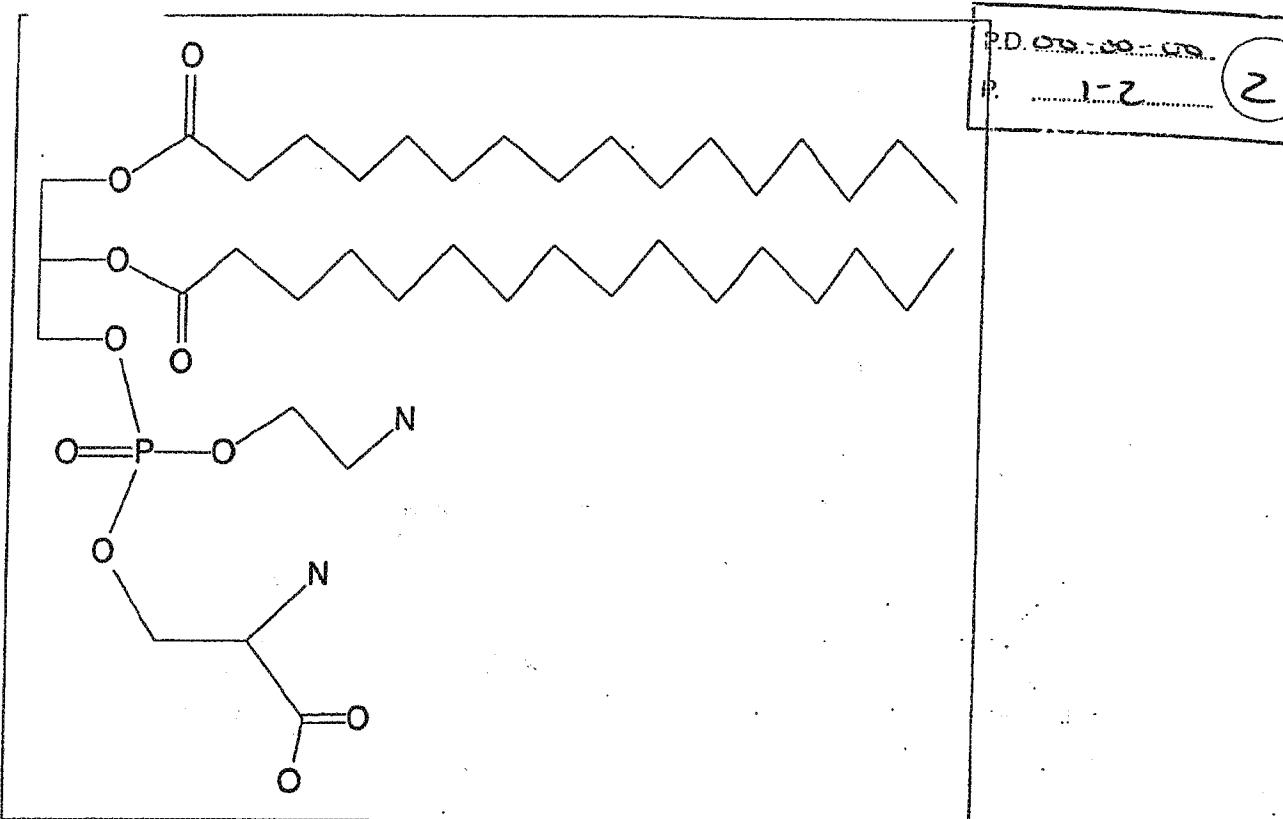
Attachments: Copies of four previously cited references

1582605_1.WPD



Substance

| | |
|---------------------------|------------------------------------------------|
| Beilstein Registry Number | 8384216 |
| Chemical Name | ethyl palmitoyl myristoyl phosphatidyl choline |
| Autoname | EPMPC |
| Linear Structure Formula | $C_{40}H_{81}NO_8P^{(1+)}Cl^{(1-)}$ |
| Molecular Formula | $C_{40}H_{81}NO_8P*Cl$ |
| Molecular Weight | 735.06, 35.45 |
| Fragment BRN | 8381555, 3587171 |
| Lawson Number | 3122, 2817, 1247, 1241, 636, 298 |
| Compound Type | acyclic |
| Constitution ID | 7118948 |
| Tautomer ID | 7903849 |
| Entry Date | 2000/03/08 |
| Update Date | 2000/03/08 |

Substance

| | |
|---------------------------|---------------------------------------------------------------------------------------------------------------------|
| Beilstein Registry Number | 6788943 |
| Chemical Name | hexadecanoic acid 2-[(2-amino-2-carboxy-ethoxy)-(2-amino-ethoxy)-phosphoryloxy]-1-hexadecanoyloxymethyl-ethyl ester |
| Autoname | hexadecanoic acid 2-[(2-amino-2-carboxy-ethoxy)-(2-amino-ethoxy)-phosphoryloxy]-1-hexadecanoyloxymethyl-ethyl ester |
| Molecular Formula | C ₄₀ H ₇₉ N ₂ O ₁₀ P |
| Molecular Weight | 779.05 |
| Lawson Number | 3549, 3122, 1241, 636 |
| Compound Type | acyclic |
| Beilstein Reference | 5-04 |
| Entry Date | 1994/11/08 |
| Update Date | 1994/12/21 |
| Compound Disposition | <u>4084653 Alternate BRN</u> |

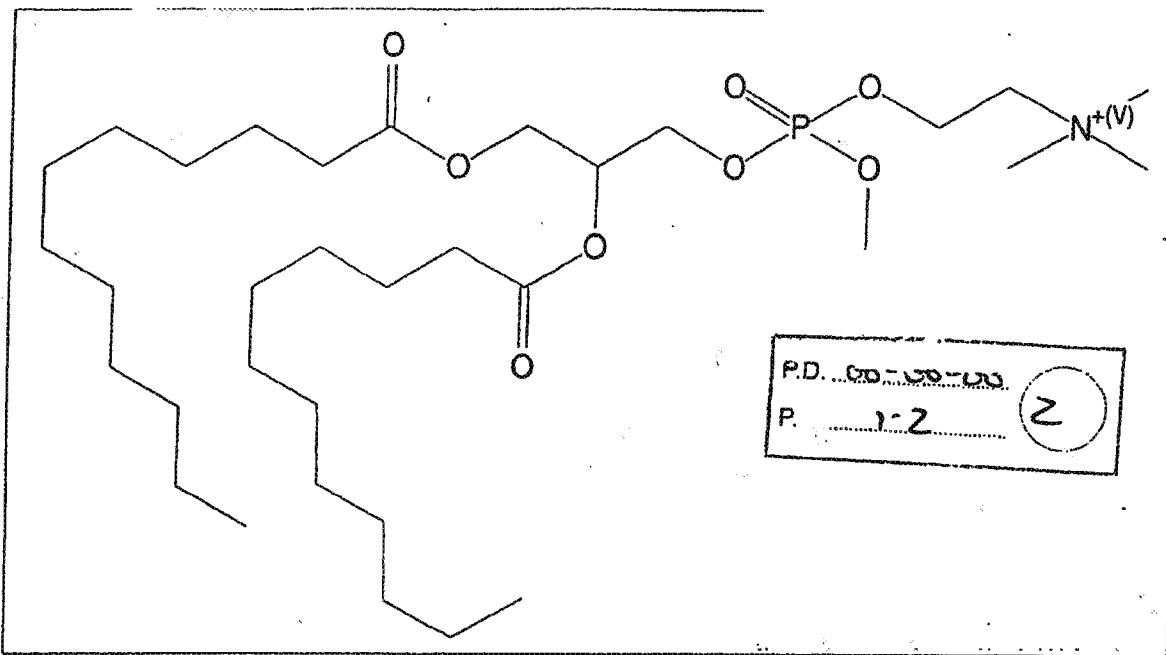
Reaction

| | |
|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reaction ID | <u>968101</u> |
| Reactant BRN | <u>1523304</u> hexadecanoic acid 2-[(2-benzyloxycarbonyl-2-benzyloxycarbonylamino-ethoxy)-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethoxy]-phosphoryloxy]-1-hexadecanoyloxymethyl-ethyl ester |
| Product BRN | 6788943 hexadecanoic acid 2-[(2-amino-2-carboxy-ethoxy)-(2-amino-ethoxy)-phosphoryloxy]-1-hexadecanoyloxymethyl-ethyl ester |
| No. of Reaction Details | 1 |
| Reaction Classification | Preparation |

| | |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Other Conditions | (i) N2H4*H2O, (ii) H2, Pd-C |
| Note 1 | Multistep reaction |
| Ref. 1 | <u>276200</u> ; Journal; Shvets, V.I. et al.; JOCYA9; J.Org.Chem.USSR (Engl.Transl.); EN; 5; 1969; 1978-1983; ZORKAE; Zh.Org.Khim.; RU; 5; 11; 1969; 2033-2039; |

Infrared Spectra

| Description | Bands |
|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ref. 1 | <u>276200</u> ; Journal; Shvets, V.I. et al.; JOCYA9; J.Org.Chem.USSR (Engl.Transl.); EN; 5; 1969; 1978-1983; ZORKAE; Zh.Org.Khim.; RU; 5; 11; 1969; 2033-2039; |



Substance

| | |
|---------------------------|--------------------------------------------------------------------------------------|
| Beilstein Registry Number | 7400057 |
| Chemical Name | 1,2-Dilaurylphosphatidylcholine methyl ester |
| Autoname | {2-[(2,3-bis-dodecanoyloxy-propoxy)-methoxy-phosphoryloxy]-ethyl}-trimethyl-ammonium |
| Linear Structure Formula | C ₃₃ H ₆₇ NO ₈ P ⁽¹⁺⁾ |
| Molecular Formula | C ₃₃ H ₆₇ NO ₈ P |
| Molecular Weight | 636.87 |
| Lawson Number | 3122, 2817, 1237, 636, 289 |
| Compound Type | acyclic |
| Constitution ID | 6396749 |
| Tautomer ID | 7081128 |
| Beilstein Reference | 6-04 |
| Entry Date | 1996/04/26 |
| Update Date | 1997/02/03 |

Reaction

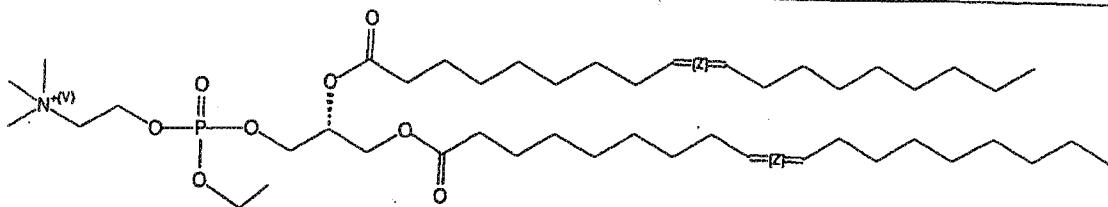
| | |
|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reaction ID | 4333536 |
| Reactant BRN | 102415 diazomethane |
| Product BRN | 4168394 1,2-Dimyristoylglycerylphosphorylcholin 7400057 {2-[(2,3-bis-dodecanoyloxy-propoxy)-methoxy-phosphoryloxy]-ethyl}-trimethyl-ammonium |
| No. of Reaction Details | 1 |
| Reaction Classification | Preparation |
| Solvent | diethyl ether |
| Time | 5 min |
| Other Conditions | Ambient temperature |

Ref. 1 [6002834](#); Journal; Harvey, D. J.; JMSPFJ; J.Mass.Spectrom.; EN; 30; 9; 1995; 1333-

1346;

Mass Spectrum

| | |
|-------------|------------------------------------------------------------------------------------------------|
| Description | spectrum |
| Note 1 | laser desorption |
| Ref. 1 | <u>6002834</u> ; Journal; Harvey, D. J.; JMSPFJ; J.Mass.Spectrom.; EN; 30; 9; 1995; 1333-1346; |



XP-002277997

Substance

| | |
|---------------------------|----------------------------------------------------------------------------------------|
| Beilstein Registry Number | 8468920 |
| Chemical Name | 1,2-dioleoyl-sn-glycero-3-ethylphosphocholine |
| Autoname | (2-[(2,3-bis-octadec-9-enyoxy-propoxy)-ethoxy-phosphoryloxy]-ethyl)-trimethyl-ammonium |
| Linear Structure Formula | C ₄₆ H ₈₉ NO ₈ P ⁽¹⁺⁾ |
| Molecular Formula | C ₄₆ H ₈₉ NO ₈ P |
| Molecular Weight | 815.18 |
| Lawson Number | 3122, 2817, 1371, 636, 298 |
| Structure Keyword | Stereo compound |
| Compound Type | acyclic |
| Entry Date | 2002/07/19 |
| Update Date | 2002/07/19 |

Pharmacological Data

| | |
|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Effect | drug interaction |
| Species or Test-System | COS-1 cells |
| Concentration | 35 mmol/l |
| Kind of Dosing | title comp.-containing gene-delivery system (carrier) prepared as emulsion (E) or liposome (L) |
| Method | cells transfected with title comp.-containing carrier-DNA complex without/with fetal bovine serum (FBS) (DNA: Escherichia coli lacZ β-galactosidase, GAL> gene) in serum-free DMEM (1 h); GAL activity measured using photometric assay |
| Further Details | title comp. effect on transfection activity (TA) studied |
| Results | TA of DNA increased; without FBS: TA(L)>TA(E); with FBS: TA(E)>TA(L) (diagram) |

Ref. 1 6329889; Journal; Kim, Tae Woo; Chung, Hesson; Kwon, Ick Chan; Sung, Ha Chin; Jeong, Seo Young; PHREEB; Pharm.Res.; EN; 18; 1; 2001; 54 - 60;